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UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF CALIFORNIA

GEN-PROBE INCORPORATED,

Plaintiff,

v.

VYSIS, INC.,

Defendant.

No. 99CV2668H AJB
JUDGE MARILYN L. HUFF

SEPARATE STATEMENT OF UNDISPUTED FACTS IN SUPPORT OF PLAINTIFF GEN-PROBE INCORPORATED'S MOTION FOR PARTIAL SUMMARY JUDGMENT

DATE: May 29, 2001
TIME: 10:30 a.m.
DEPT.: Courtroom 1

Plaintiff Gen-Probe, Incorporated respectfully submits the following statement of undisputed material facts, together with references to supporting evidence, in support of its motion for partial summary judgment.

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UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
1. United States Patent No. 5,750,338 (the '338 patent) consists of the specification, including drawings, and the claims. The '338 patent contains six independent claims (claims 1, 7, 19, 27, 28 and 34). Each of these claims is generally directed to a method of, or a kit for, amplifying and/or detecting a target polynucleotide (i.e., a nucleic acid), wherein the target is first isolated on a support.	'338 Patent, Exhibit 8[1]
2. Each of the claims contains a step of "amplifying" the target polynucleotide or sample. For example, claim 1 provides: 1. A method for amplifying a target polynucleotide contained in a sample comprising the steps of: (a) contacting the sample with a first support which binds to the target polynucleotide; (b) substantially separating the support and bound target polynucleotide from the sample; and (c) *amplifying* the target polynucleotide.	'338 Patent, Exhibit 8 at col. 32, ll. 27 to 32, (emphasis added).
3. The '338 patent specification sets forth seven examples of the methods taught by the inventors. The first three examples refer only to methods of target capture alone, and do not	'338 Patent, Exhibit 8, at col. 30, ll. 14-18, (emphasis added).

[1] Unless otherwise specified, all references to Exhibits shall refer to the exhibits attached to the Notice of Lodgment of Exhibits filed concurrently herewith.

UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
refer to amplification. The last four examples refer to combining target capture and methods of amplification. Between the end of target capture examples and the start of the amplification examples, the inventors expressly set forth their teachings with respect to amplification methods. Referring to the target capture methods described in Examples 1 through 3, the inventors stated: The sensitivity of the above DNA or RNA target capture methods can be enhanced by amplifying the captured nucleic acids. This can be achieved by ***nonspecific replication using standard enzymes*** (polymerases and/or transcriptases).	
4. The '338 patent makes it clear that the reference to non-specific amplification methods was intentional and pointed out that one of the express benefits of their invention was that it permitted the use of non-specific enzymes and non-specific primers: Amplification of the target nucleic acid sequences, because it follows purification of the target sequences, can employ **non-specific** enzymes or primers. **Thus no specifically tailored primers are needed for each test, and the same standard reagents can be used, regardless of targets.**	'338 Patent, Exhibit 8 at col. 30, ll. 30-40, (emphasis added).

UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
5. The '338 patent specification sets forth four examples of the amplification methods contemplated by the inventors (Examples 4-7). Consistent with the teaching of the patent that sequence-specific primers and specific enzymes are not necessary, each example suggests and describes amplification methods that use only non-specific primers and enzymes.	'338 Patent, Exhibit 8, at col. 30, ll. 44-45.
6. Example 4 illustrates "the use of RNA polymerase to amplify target DNA." It describes a method for amplifying the capture DNA by non-specific amplification using polymerases that lack transcriptional specificity.	'338 Patent, Exhibit 8, at col. 30, l. 59 to col. 31, l. 17.
7. Example 4 discloses only non-specific amplification:	Lawrie Depo., Exhibit 9 at 231:7-13, emphasis added.
8. Example 5 describes a non-specific amplification method in which the target DNA is replicated using random (*i.e.*, non-specific) primers and non-specific transcription of that DNA into RNA: In this example, both non-specific replication of target DNA and transcription of that DNA are used to amplify capture target DNA... .. Because the primers are *random*, some will, simple (sic) as a matter of statistics, bind to and cause replication of sample sequences, no matter what those sequences are	'338 Patent, Exhibit 8, at col. 31, l. 24-54, emphasis added.

UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
9. Example 5 discloses only non-specific amplification.	Lawrie Depo., Exhibit 9, at 231:14-16; Richards Depo., Exhibit 10, at 139:23 – 140:3.
10. Example 6 describes replication of target DNA using DNA polymerase and *random* hexamer oligonucleotides "to bring about *non-specific* double-stranded DNA synthesis" using a series of repeated heat denaturation and enzyme replacement steps	'338 Patent, Exhibit 8, at col. 31, l. 3 to col. 32, l. 19.
11. Example 6 discloses only *non-specific* amplification.	Lawrie Depo., Exhibit 9, at 231:17-19; Richards Depo., Exhibit 10, at 140:9-13.
12. Example 7 describes *non-specific* amplification using an RNA polymerase, Qß replicase: In this example, rRNA and RNA transcribed from target DNA is purified using a capture probe, described above. The hybrid duplex is then denatured and single stranded nucleic acids are then replicated *non-specifically* using Qß replicase…	'338 Patent, Exhibit 8, at col. 32, l. 10-19.
13. Example 7 discloses only nonspecific amplification.	Lawrie Depo., Exhibit 9, at 231:20–22; Richards Depo., Exhibit 10, at 141: 3-7.
14. The first pages of the '338 patent provide drawings of various methods encompassed by the invention.	'338 Patent, Exhibit 8.
15. The first 3 drawings (Figure 1a to Figure 3) depict target capture methods alone, without amplification.	'338 Patent, Exhibit 8.

UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
16. Figures 4, 5 and 6 depict target capture followed by amplification using only non-specific primers or enzymes.	'338 Patent, Exhibit 8.
17. The drawings included in the patent are discussed and described in the text of the patent specification	'338 Patent, Exhibit 8, at cols. 10 - 19.
18. The text of the specification expressly states that in each of the drawings that include amplification (Figures, 4, 5 and 6) "the isolated target is *non-specifically* amplified to form a multitude of amplification products."	'338 Patent, Exhibit 8. at col. 15, ll. 56-58, emphasis added.
19. One of ordinary skill in the art would have understood the term "amplifying" in the '338 patent to include only the non-specific amplification methods taught by the patent.	Falkinham Declaration at ¶¶ 5 - 52.
20. One of ordinary skill in the art would not have understood the term "amplifying" to include other amplification methods that use sequence-specific primers or enzymes.	Falkinham Declaration at ¶ 5.
21. The PCR method was first described at a scientific meeting in the summer of 1985 and was published in December 20, 1985.	Saiki et al., "Enzymatic amplification of beta-globin genomic sequences and restriction site analysis for diagnosis of sickle cell anemia," SCIENCE 230:1350-54 (1985).
22. Within the scientific community, PCR was immediately "big news."	Richards Depo, Exhibit 10, at 38:6-8.

UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
23. The patent was meant to cover *new* amplification methods using non-specific primers, not already-known methods such as PCR.	Lawrie Depo., Exhibit 9, at 178:19 - 180:11; 180:23 – 181:13.
24. On December 15, 1989, Dr. James C. Richards, the Director of Business Development and Licensing for Gene-Trak Systems, admitted that the '338 patent encompassed only amplification with non-specific primers and explicitly contrasted the methods of the patent with other methods of amplification using specific primers. Dr. Richards' analysis was set forth in a letter to one of Gene-Trak's partners, Amoco Technology Company.	Exhibit 1
25. Dr. Richards first discussed the fact that the pending patent application encompassed the use of random, non-specific primers. He then discussed the effect of combining non-specific amplification with the use of an initial target capture step. Finally, he pointedly contrasted the invented method with other known methods that used specific primers or promoters (e.g., enzymes): Cetus, Sibia/Salk, Biotechnica, etc. all claim **specific** primers for amplification whereas the present invention claims uses of the opposite, namely, **non-specific**	Exhibit 1 at p. 2 (emphasis in original).

UNDISPUTED MATERIAL FACTS:	SUPPORTING EVIDENCE:
primer or promoters.... Following extensive washing, captured target polynucleotides could be released and the non-specific amplification process could take place.	
26. Gen-Probe's HIV-1/HCV Assay use a target-specific amplification technology called Transcription-Mediated Amplification (TMA).	Longiaru Declaration at ¶ 5.
27. TMA uses *specific* primers, *specific* promoters, and a *specific* polymerase enzyme that recognizes only those promoters.	Longiaru Declaration at ¶¶ 6-11.
28. Gen-Probe's product does not use non-specific amplification.	Longiaru Declaration at ¶¶ 6-11.

Dated: April 30, 2001

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